INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Effectiveness of antihypertensive drugs to prevent cognitive decline, mild cognitive impairment, and dementia. An overview of systematic reviews

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Review question / Objective: **To determine effectiveness of antihypertensive drugs to prevent different dementia subtypes such as Alzheimer's disease and vascular dementia.**
Condition being studied: **Dementia is a global health burden, with the number of affected individuals increasing. A recent meta-analysis reported that the prevalence of all-type dementia was 697 per 10,000 people and the prevalence of Alzheimer's disease was 324 per 10,000 people. The SHEP and SYST-EUR were the two first randomized controlled trials to show that hypertension treatment reduces dementia risk.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 December 2022 and was last updated on 14 December 2022 (registration number INPLASY2022120057).

INTRODUCTION

Review question / Objective: **To determine effectiveness of antihypertensive drugs to prevent different dementia subtypes such as Alzheimer's disease and vascular dementia.**

Rationale: **While several systematic reviews have reported that antihypertensive drugs reduce dementia risk, others could not support these findings. Consequently, we believe it is necessary to compile the evidence from systematic reviews in an overview.**

Condition being studied: **Dementia is a global health burden, with the number of affected individuals increasing. A recent meta-analysis reported that the prevalence of all-type dementia was 697 per 10,000 people and the prevalence of Alzheimer's disease was 324 per 10,000 people. The SHEP and SYST-EUR were the two first**

randomized controlled trials to show that hypertension treatment reduces dementia risk.

METHODS

Search strategy: We used the following medical subject headings (MeSH) to develop the search strategy: 'antihypertensive drugs', 'diuretics', 'Angiotensin II receptors blockers', and 'Angiotensin-converting enzyme inhibitors', 'calcium channels blockers', 'beta-adrenergic blockers', 'cognitive decline', 'mild cognitive impairment', 'dementia', 'vascular dementia', 'Alzheimer's disease'. We used the following limits: "Meta-Analysis", "Systematic Reviews", "Humans".

Participant or population: Patients had to have levels of systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg regardless of age or history of cerebrovascular disease, and who take antihypertensive drugs.

Intervention: Antihypertensive drugs.

Comparator: Placebo, any other antihypertensive drug, or other control intervention.

Study designs to be included: Systematic reviews of randomized controlled trials (RCT) or prospective cohort studies.

Eligibility criteria: Systematic reviews of randomized controlled trials (RCT) or prospective cohort studies.

Information sources: Cochrane Library, MEDLINE/PubMed, EMBASE, and PROSPERO.

Main outcome(s): Risk of developing cognitive decline, mild cognitive impairment, dementia, Alzheimer's disease, and vascular dementia.

Quality assessment / Risk of bias analysis: The risk of bias in each included review will be assessed using the Risk of Bias in Systematic Reviews (ROBIS) tool, and the quality of the evidence will be assessed according to the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach.

Strategy of data synthesis: The results will be shown as tables and figures. To respond to the aim of this overview, we performed a reanalysis of the data for each outcome. Because of the overlapping information in the systematic reviews, the first step was to create a citation matrix to visually demonstrate the amount of overlap and then select the RCT that properly adjusted to the inclusion criteria. Statistical heterogeneity between studies will be assessed with I2 statics. If severe heterogeneity will be identified, a random effects model will be used rather than a fixed effects model with an inverse variance method to calculate the pooled RR.

Subgroup analysis: None.

Sensitivity analysis: None.

Language restriction: No restrictions shall be imposed on the language of publication.

Country(ies) involved: Chile.

Keywords: Alzheimer Disease; Antihypertensive Agents; Cognitive dysfunction; Dementia; Preventive Medicine.

Dissemination plans: The findings of this overview will be presented at conferences and published in a peer-reviewed journal.

Contributions of each author:

Author 1 - Federico Fillipin - Conception of the research idea and design of the protocol.
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